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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,759	12/08/2003	David John King	CARP0007-101	4275

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COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
04/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,759	KING ET AL.	
	Examiner	Art Unit	
	PARITHOSH K. TUNGATURTHI	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/214,251.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/28/2008 has been entered.

2. Claims 1-10 have been cancelled.

3. Claim 11 has been amended.

4. Claims 11-16 are under examination.

5. This office action contains New Grounds of Rejections.

Rejections Withdrawn

6. The rejection of claims 11-14 under 35 U.S.C. 102(b) as being anticipated by Zapata[a] et al (FASEB J. 1995. 9:A1479; IDS – 12/13/2004) is withdrawn in view of amendments to the claim.

7. The rejection of claims 11-16 under 35 U.S.C. 103(a) as being unpatentable over Zapata[a] et al (FASEB J. 1995. 9:A1479) and further in view of Zapata[b] et al (U.S. Patent 6214984, Continuation Date 04/20/1995; IDS – 12/13/2004).

8. The rejection of claims 11-16 under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al (U. S. Patent 5,853,723, filed 9/20/96; IDS – 12/13/2004) and further in view of Bodmer et al (WO 89/01974, published 3/9/89; IDS – 12/13/2004) is withdrawn in view of applicants arguments.

The applicant stated that Bodmer et al and the present application were both owned by, or subject to assignment to, the same entity at the time the invention the subject of the present application was made (please see page 5 of the response filed 11/29/2007, in particular).

Priority

9. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/214,251, filed on 03/10/1999.

New Grounds of Rejections

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zapata[a] et al (FASEB J. 1995. 9:A1479; IDS-12/13/2004) in view of Griffiths et al (U.S. Patent 5,670,132, Date Filed: 09/20/1994; IDS – 12/13/2004).

Claims 11-14 are drawn to a modified monovalent antibody fragment which is a Fab' wherein the CH1 is extended to provide a hinge domain which contains only one cysteine residues which is covalently linked through it sulphur atom to a polymer molecule, wherein said polymer molecule has an average molecular weight of from about 25,000 Da to about 40,000 Da, wherein the polymer is a substituted, straight or branched chain polyalkelene, poly(ethylene glycol), methoxy(polytheylene glycol). Claims 15 and 16 are drawn to an antibody fragment of claim 11 covalently attached to one or more effector or reporter molecules and a pharmaceutical composition comprising such antibody fragment with one or more pharmaceutically acceptable excipients, diluents or carriers.

Zapata[a] et al teach a Fab' fragment which contains a single cysteine in the hinge region including the coupling of monomethoxypoly(ethylene glycol) to the cysteine. Zapata[a] et al does not teach the polymer of 25,000 Da to about 40,000 Da, and a composition with a carrier or fragment with an effector or reporter molecule. These deficiencies are made up for in the teachings of Griffiths et al.

Griffiths et al teach site specific conjugation of PEG to Fab or Fab' (see column 2, lines 46-58) outside the variable region (see column 3 and 4), wherein the molecular weight of the PEG can be 30,000 Da (column 3, lines 12-19 in particular); particularly Griffiths et al further teach an antibody conjugated to 1-10 PEG-5,000 moieties (i.e. 5000 Da to 50, 000 Da) to reduce renal uptake and retention of the PEGylated antibody fragment after radiolabeling (claim 15 and 16, in particular). In addition, Griffiths et al teach that the antibody fragment has an effector attached (see abstract) including compositions comprising such antigen binding fragments and a pharmaceutically acceptable carrier (column 6, lines 62-67 in particular).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a Fab' fragment covalently linked to a polymer molecule, having an average molecular weight of from about 25,000 Da to about 40,000 Da; and a Fab' fragment covalently attached to an effector molecule including pharmaceutical compositions comprising such antibody fragments.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success to have produced a Fab' fragment covalently linked

to a polymer molecule, having an average molecular weight of from about 25,000 Da to about 40,000 Da; and a Fab' fragment covalently attached to an effector molecule including pharmaceutical compositions comprising such antibody fragments because Zapata[a] et al teach a Fab' fragment which contains a single cysteine in the hinge region including the coupling of monomethoxypoly(ethylene glycol) to the cysteine and because Griffiths et al teach site specific conjugation of PEG to Fab or Fab', wherein the molecular weight of the PEG can be 5000 Da to 50, 000, in addition to teaching antibody fragments attached to an effector molecule, including compositions comprising such antigen binding fragments and a pharmaceutically acceptable carrier.

Thus, since Zapata[a] et al recognize that the ability to modify the clearance rate of an antibody Fab' fragment by attaching MePEG moiety at a unique site, without affecting antigen binding, increases significantly the potential therapeutic value of this type of molecule and Griffiths et al teach that conjugation of 1-10 PEG-5,000 moieties (i.e. 5000 Da to 50, 000 Da) reduces renal uptake and retention of the PEGylated antibody fragment after radiolabeling, one of ordinary skill in the art would be motivated and would have a reasonable expectation of success to develop, in the interest of developing a more effective therapeutic strategy, to substitute the single PEG moiety of Zapata[a] et al with a polymer of 25,000 Da to 40,000 Da as taught by Griffiths et al and further produce Fab' fragments covalently attached to an effector molecule including pharmaceutical compositions comprising such antibody fragments as taught by Griffiths et al. Thus, a person of ordinary skill in the art, facing the wide range of needs created by the developments in the field of endeavor, would have seen a benefit to develop a

Fab' fragment covalently linked to a polymer molecule, having an average molecular weight of from about 25,000 Da to about 40,000 Da.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

12. No claims are allowed

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
Ph: (571) 272-8789

/David J Blanchard/
Primary Examiner, Art Unit 1643